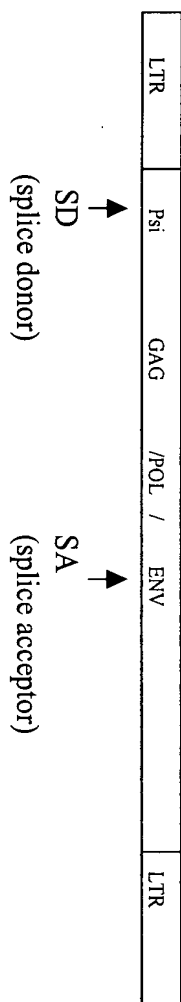
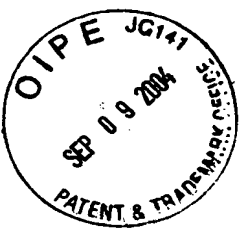
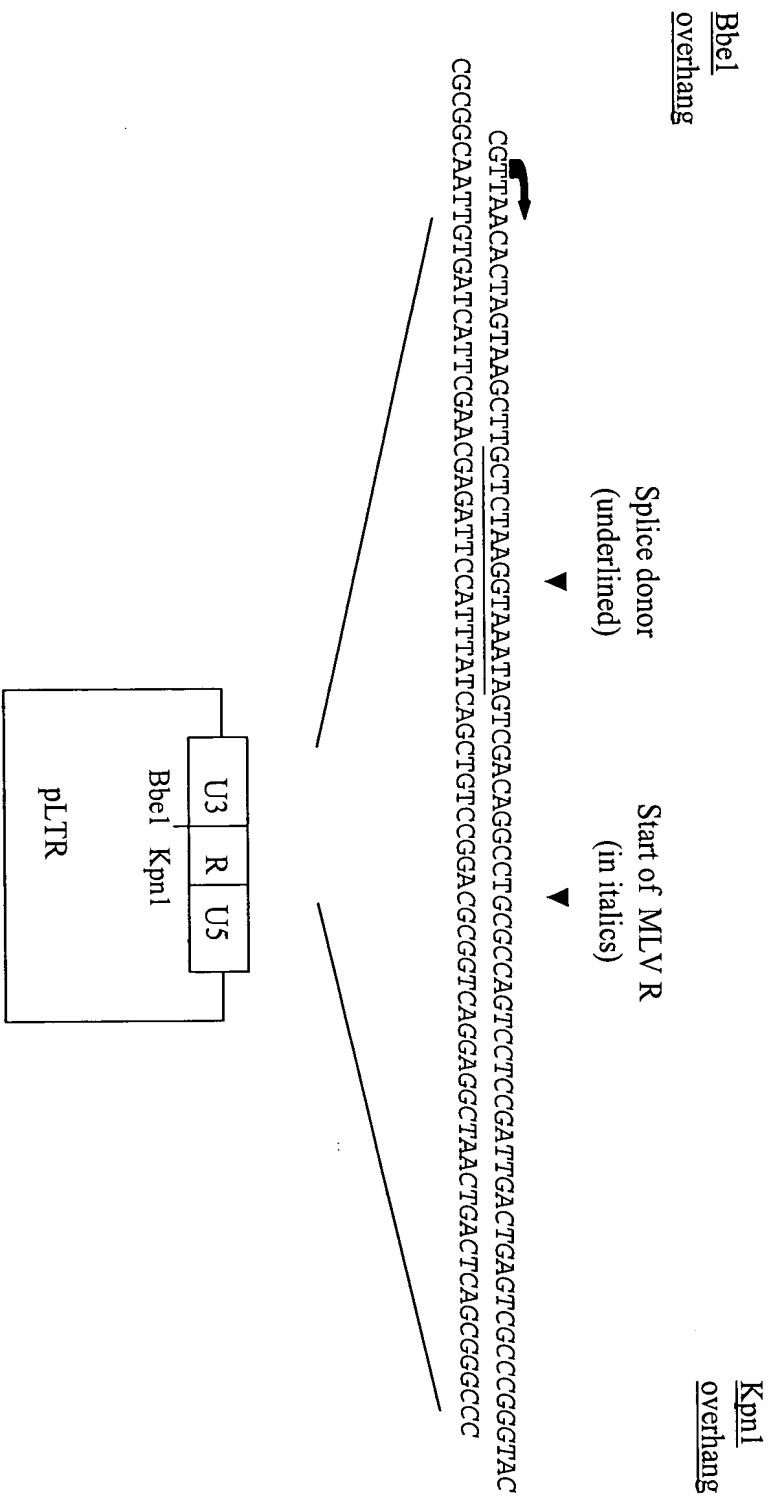


Figure 1



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Figure 2



**Figure 3**

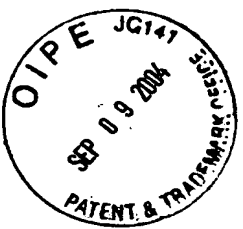
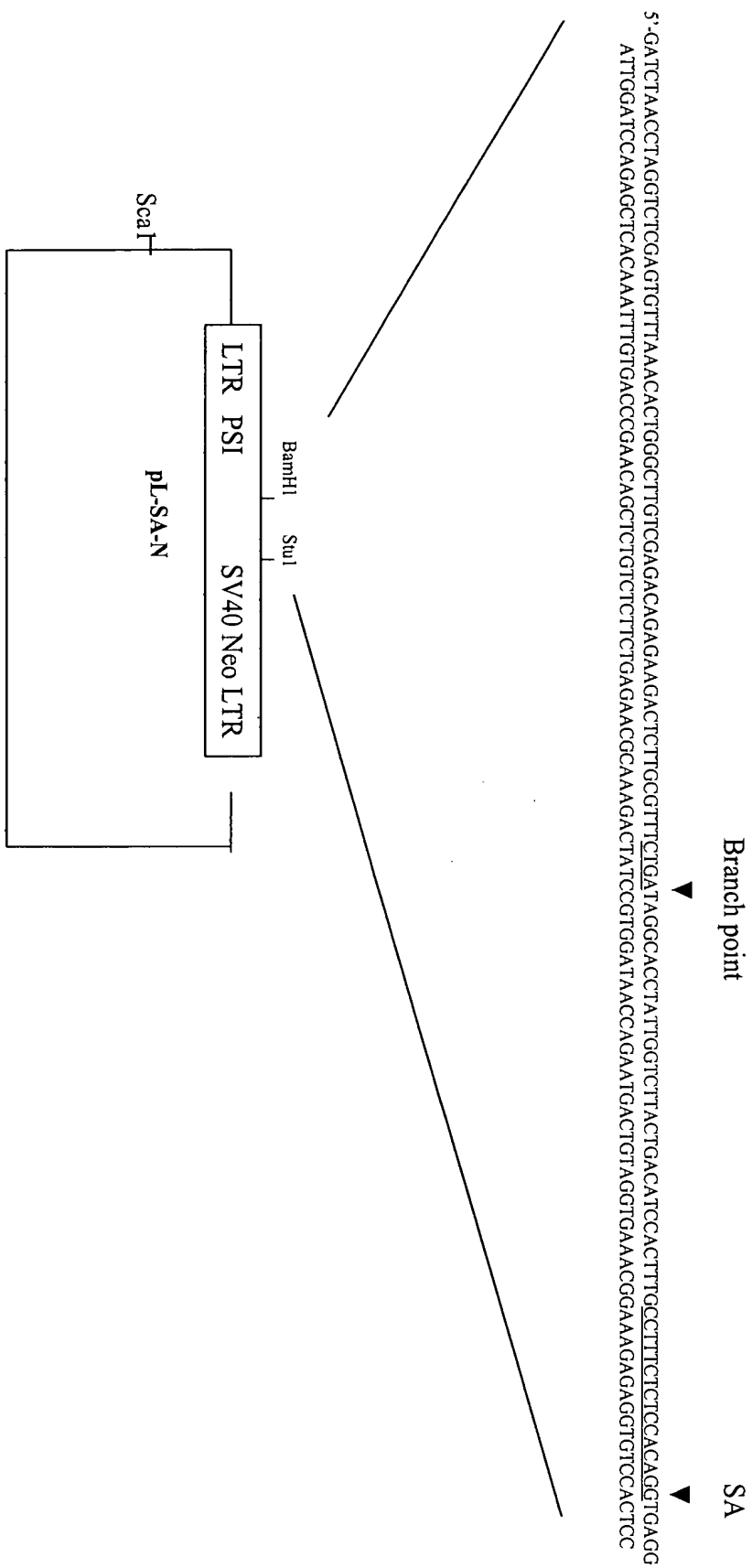
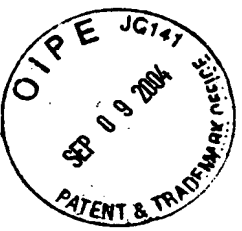
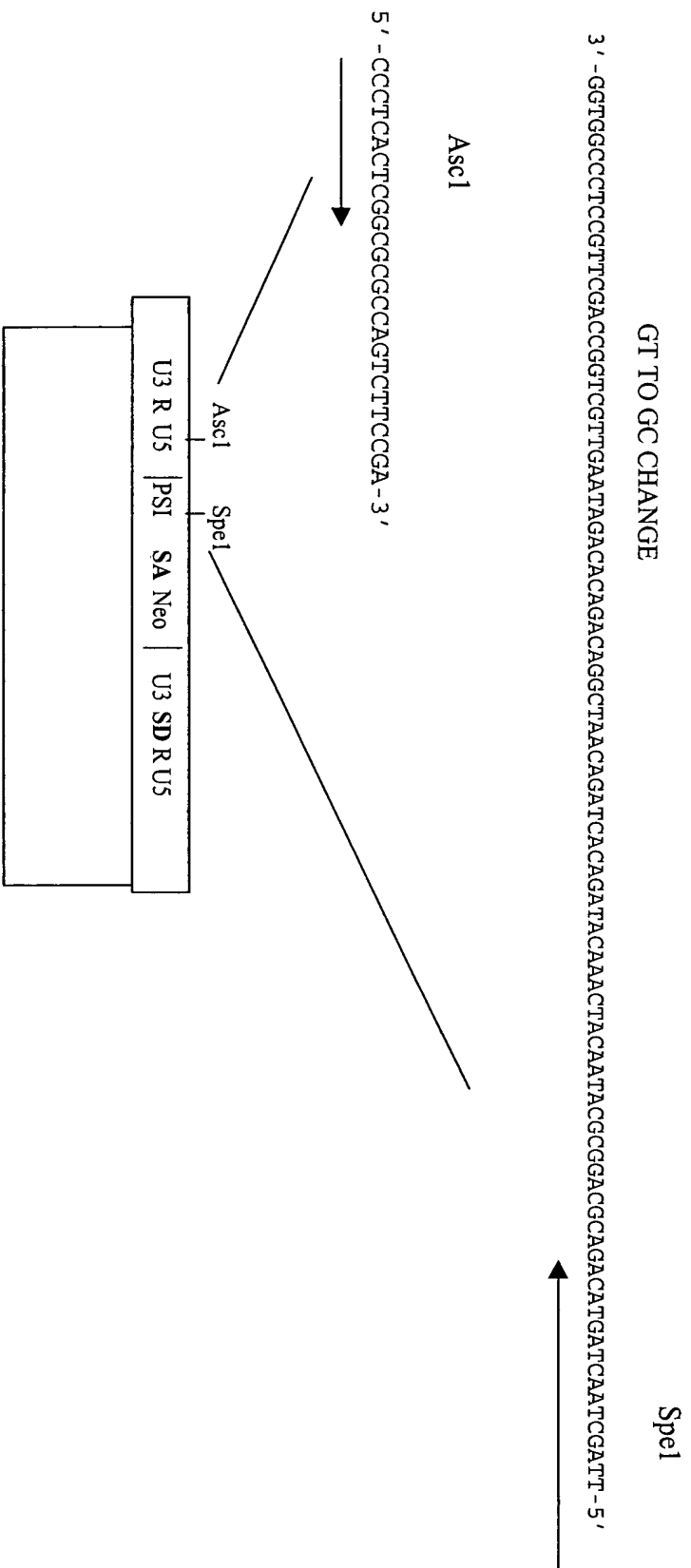


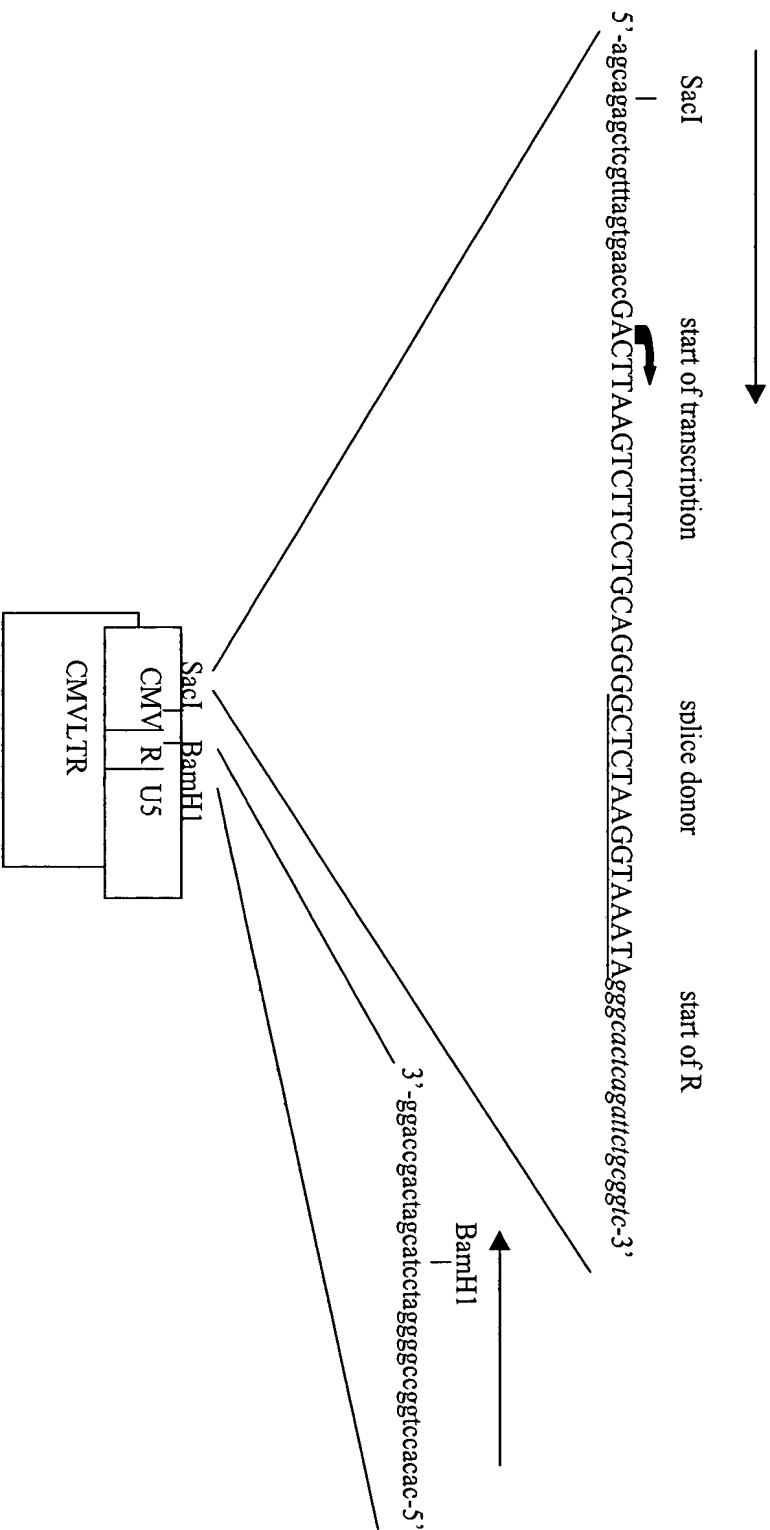
Figure 4



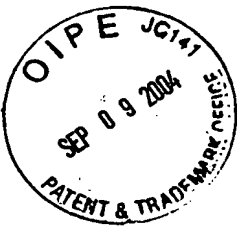
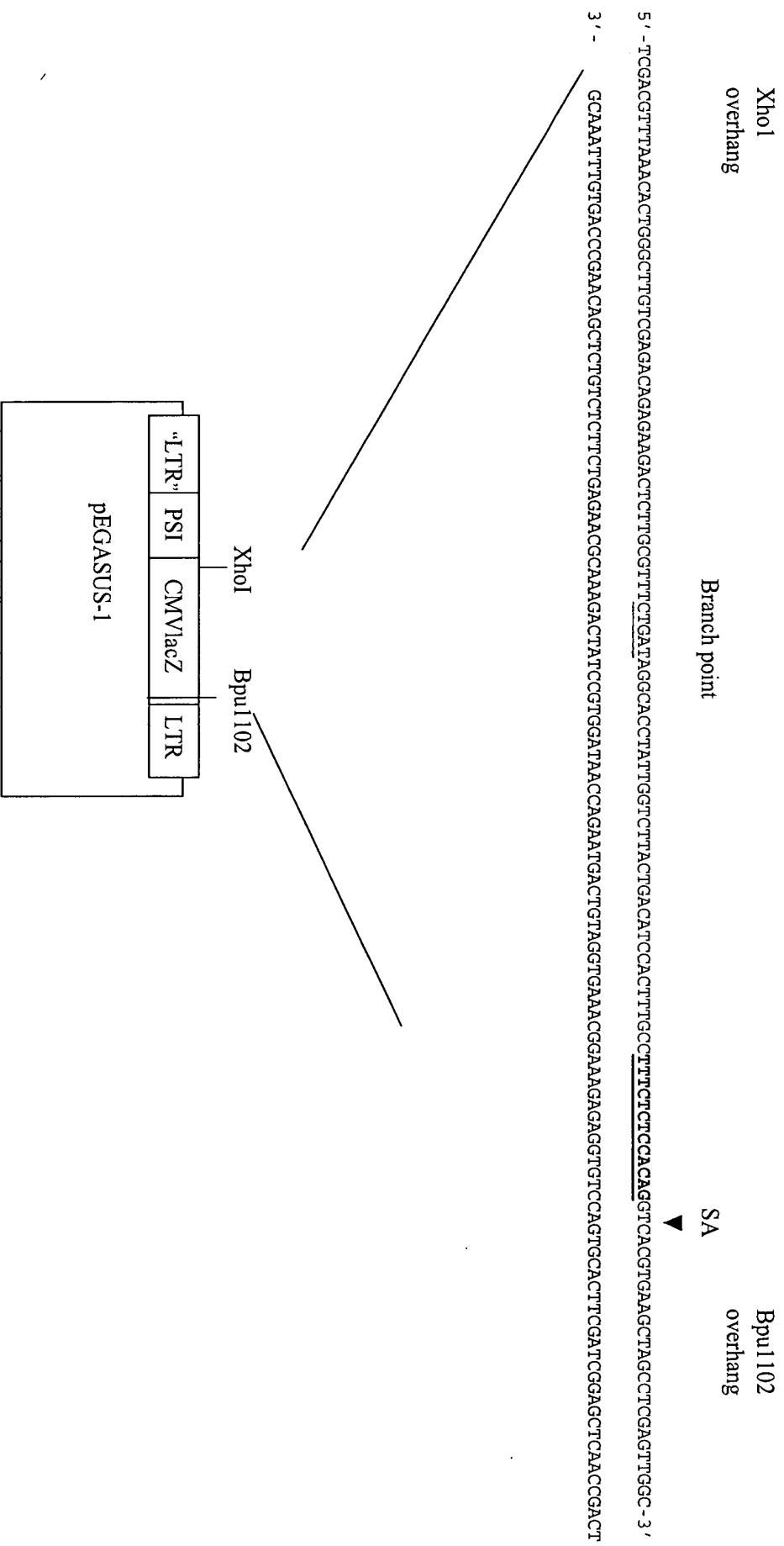
## Figure 5



Figure 6



**Figure 7**



100





**Figure 9**

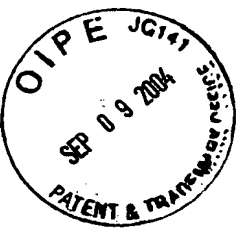
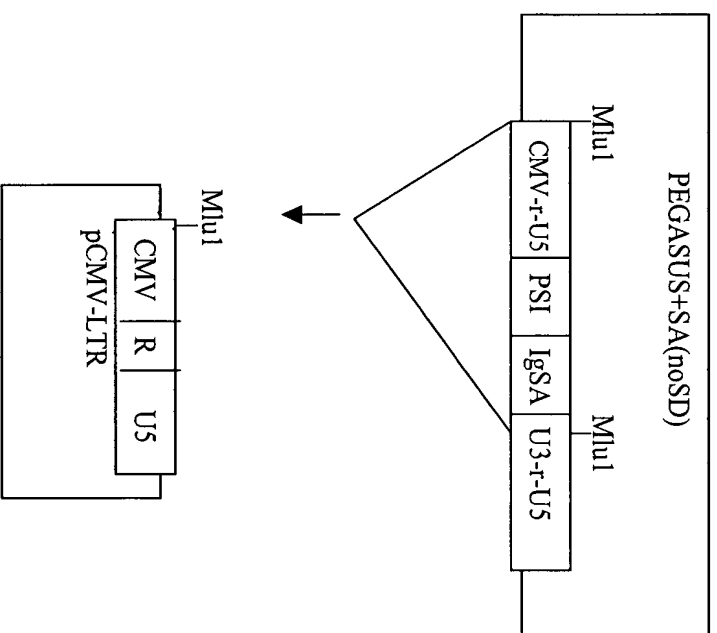
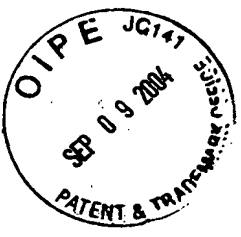
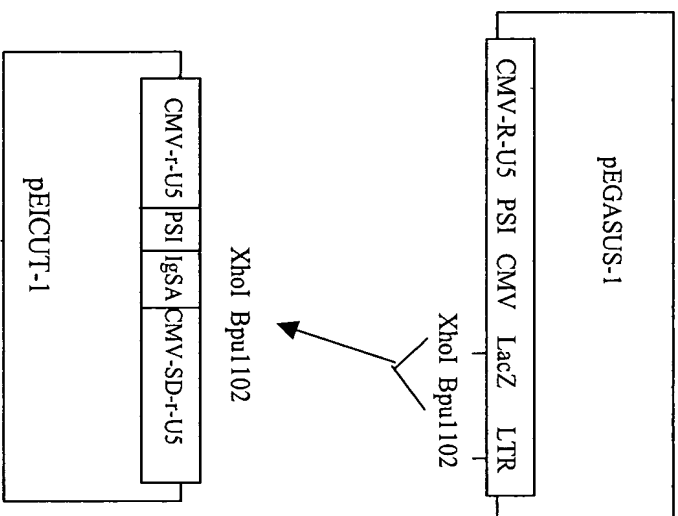


Figure 10



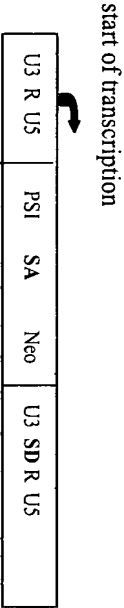
[illegible]

[illegible]



Figure 12

(A) pICUT vector in transfected cells



(B) pICUT vector in transduced cells

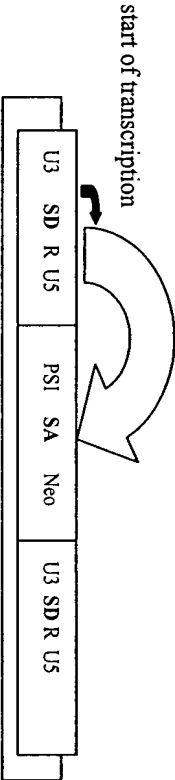
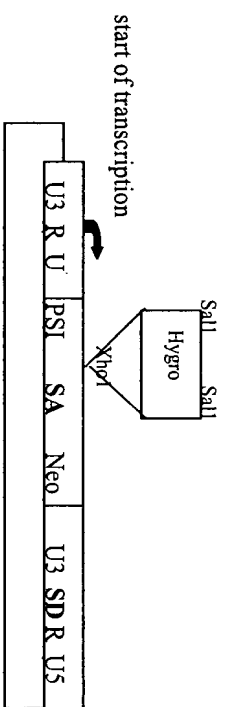


Figure 13

(A) Vector configuration in transfected cells



(B) Vector configuration in transduced cells

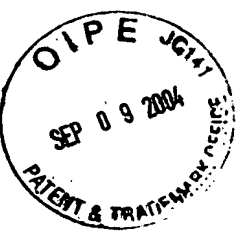
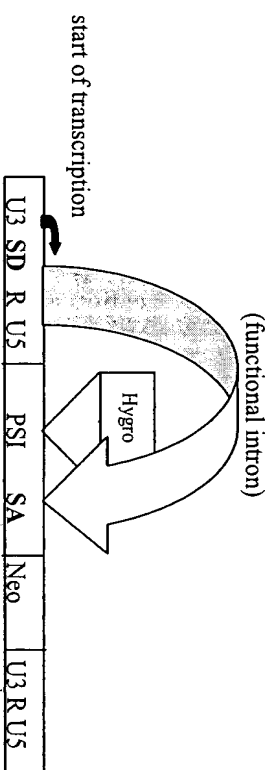
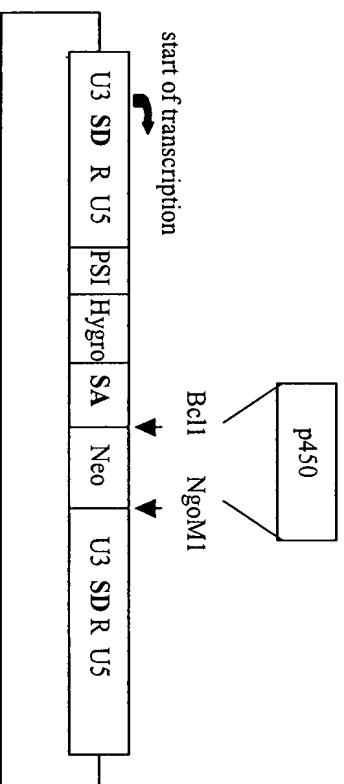
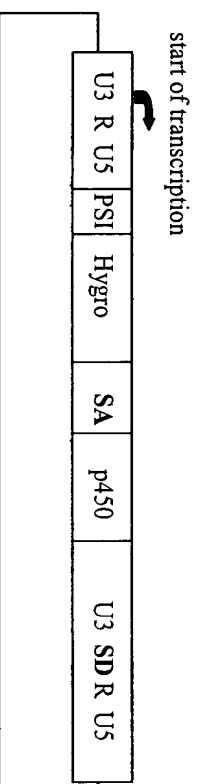


Figure 14

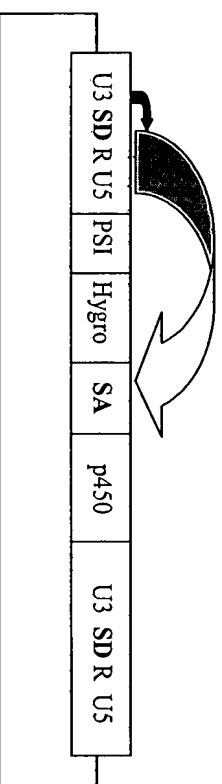
(A) p450 insertion



(B) Hygromycin expression in transfected cell



(C) p450 expression in transduced cell



**Figure 15**

3'end of pol	5'-ATG CGT TCA ACG CTC TCA AAA CCC CTT AAA AAT AAG
5'altered 4070A	5'-ATG GCC AGA AGC ACC CTG AGC AAG CCA CCC CAG GAC
	GTT AAC CCG CGA GGC CCC CTA ATC CCC-3'
	AAA AAT CCC TGG AAA CCT CTG ATC GTC-3'





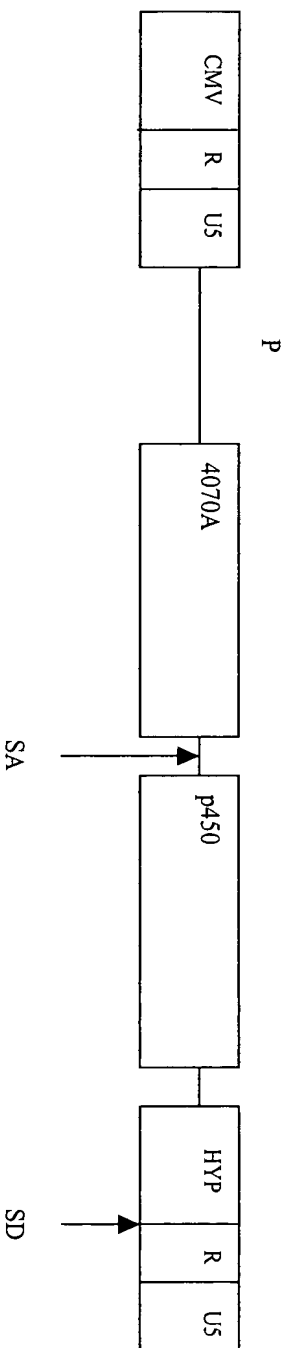
Figure 16

ATGGCCAGAA GCACCCCTGAG CAAGCCACCC CAGACAAAA TCAATCCCTG GAAACCTCTG  
ATCGTCATGG GAGTCCTGTT AGAGTAGGG ATGGCAGAGA GCCCCATC AGGTC  
TTTAATGTAA CCTGGAGAGT CACCAACCTG  
ATGACTGGGC GTACCGCCAA TGCCACCTCC CTCCTGGGAA CTGTACAAGA TGCCTTCCCA  
AAATTATAT TTAGTCTATG TGAATGTGTC GGAGAGAGT GGGACCTTC AGACCAGGAA  
CCGTATGTCG GGTATGGCTG CAAGTACCCC GCAGGGAGAC AGCGGACCCG GACTTTGAC  
TTTTACGTGT GCCCTGGGCA TACCGTAAAG TCGGGGTGTG GGGACCCAGG AGAGGGCTAC  
TGTGTAAT GGGGTGTGA AACACCGGA CAGGCTTACT GGAAGCCAC ATGATCGTG  
GACCTAATCT CCTTAAGCG CGGTACACC CCTGGGACA CGGATGCTC TAAAGTTGCC  
TGTGGCCCT GCTACGACCT CTCCAAGTA TCCAATTCT TCCAAGGGG TACTCGAGG  
GGCAGATGCA ACCCTTAGT CTTAGAATTC ACTGATGCAG GAAAAAGGC TAACTGGGAC  
GGGCCCAAT CGTGGGACT GAGACTGTAC CGACAGGAA CAGATCTTAT TACCATGTTT  
TCCCTGACCC GGCAGGTCT TAAATGGGA CCCGAGTCC CCATAGGGC CAACCCAGTA  
TTACCCGACC AAAGACTCCC TTCCTCACCA ATAGAGATTG TACCGGCTCC ACAGCCACT  
AGCCCCCTCA ATACAGTTA CCCCCCTCC ACTACAGTA CACCTCAAC CTCCCCTACA  
AGTCCAAGTG TCCACAGCC ACCCCAGGA ACTGAGATA GACTACTAGC TCTAGTCAA  
GGAGCCTATC AGCGCTTAA CTTACCAAT CCCGACAAGA CCCAAGATG TTGCTGTGC  
TTAGTGTGG GACTTCCTTA TTACGAAGA GTAGCGGTG TGGCACTTA TACCAATCAT  
TCCACCGCTC CGGCCAATG TAGGCCACT TCCACACATA AGCTTACCCT ATCTGAAGTG  
ACAGACAGG GCTATGCAT GGGGACAGTA CCTAAATC ACCAGGCTT ATGTAACAC  
ACCCAAGCG CCGCTCAG ATCCTACTAC CTTGACGAC CCGCCGAC AATGTGGCT  
TGCAGCACTG GATTGACTCC CTGCTGTCC ACCACGTC TCAATCTAAC CACAGATTAT  
TGTATATTAG TTGAACCTG GCCCAGAGTA ATTTACCACT CCCCAGTTA TATGTATGTT  
CAGCTTGAC AGCGTACCAA ATATAAAGA GAGCAGTAT CATTGACCT GGCCTTTTA  
CTAGGAGGAT TAACCATGG AGGAATTGA GCTGGAATAG GACGGGGAC CACTGCCTTA  
ATTAAGCCC AGCAGTTGA GCAGTTCAT GCCGTATCC AGACAGCT CAACGAGTC  
GAAAAGTCAA TTACCAACCT AGAAAGTCA CTGACCTCGT TGTCTGAAGT AGTCTACAG  
AACCGCAGAG GCTAGATT TGTATTCCTA AAGGAGGAG GTCTGTGCG AGCCTTAAA  
GAAGAATGTT GTTTTATGC AGACACACG GGGTAGTGA GAGACAGCAT GGCCAATTA  
AGAGAAAGGC TTAATCAGAG ACAAAAATA TTTGAGACAG GCCAAGGATG GTTCGAAGGG  
CTGTTTAATA GATCCCCCTG GTTTACACC TTAATCTCA CCATCATGGG ACCTTAATA  
GTACTCTTAC TGAATCTACT CTTGAGACCT TGCATCTCA ATGATTTGTT CCAATTTGTT  
AAAGACAGGA TCTCATGTT CAGGCTCTG GTTTGACTC AGCAATATC CCAGCTAAA  
CCCATAGAGT ACGAGCATG A

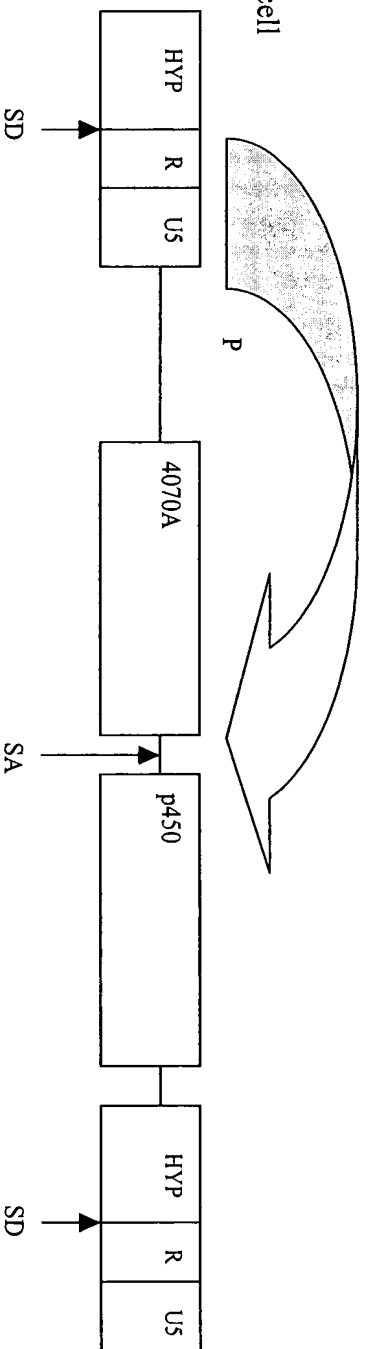


**Figure 17**

Packaging cell



Transduced cell



CMV=CMV Promoter  
HYP= Hypoxia responsive promoter  
P= MLV packaging signal  
4070A= MLV amphotrophic Env gene  
p450= p450 reductase encoding cDNA  
SD= Splice donor  
SA= Splice acceptor

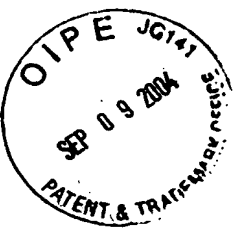


Figure 18

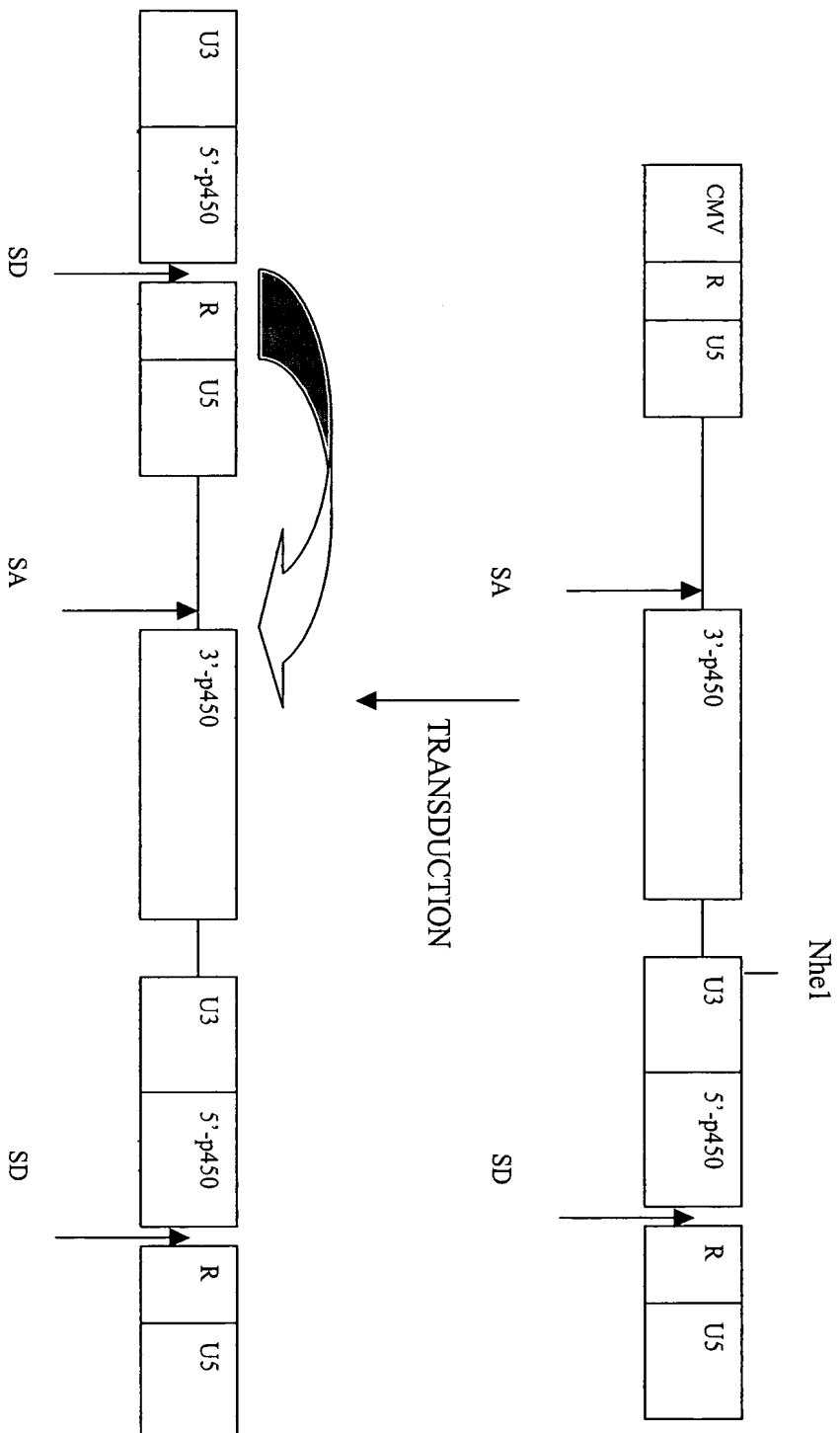


Figure 19

Transfer vector (shown linear)

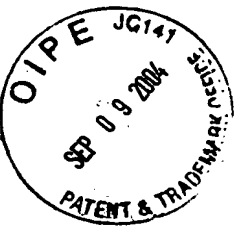
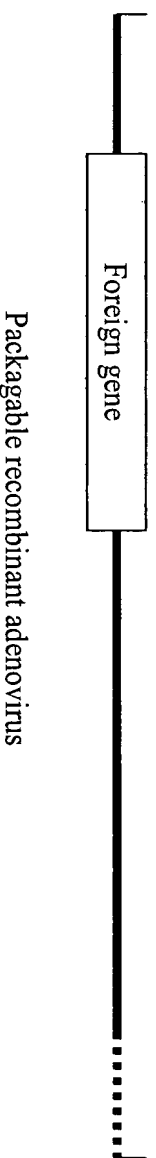
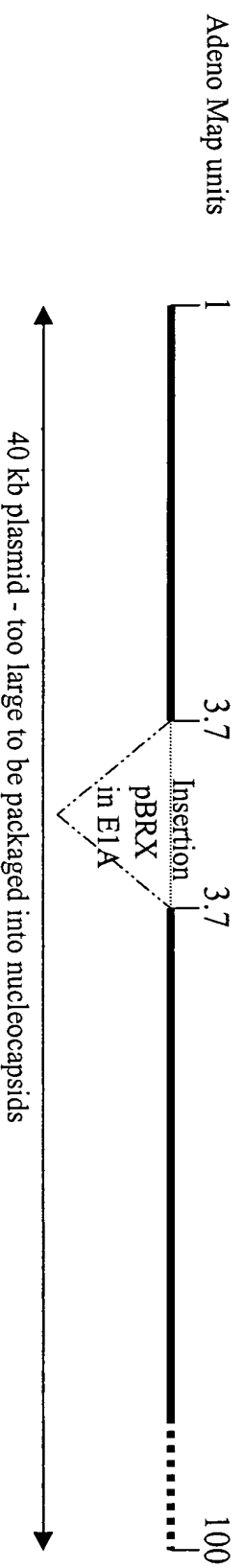
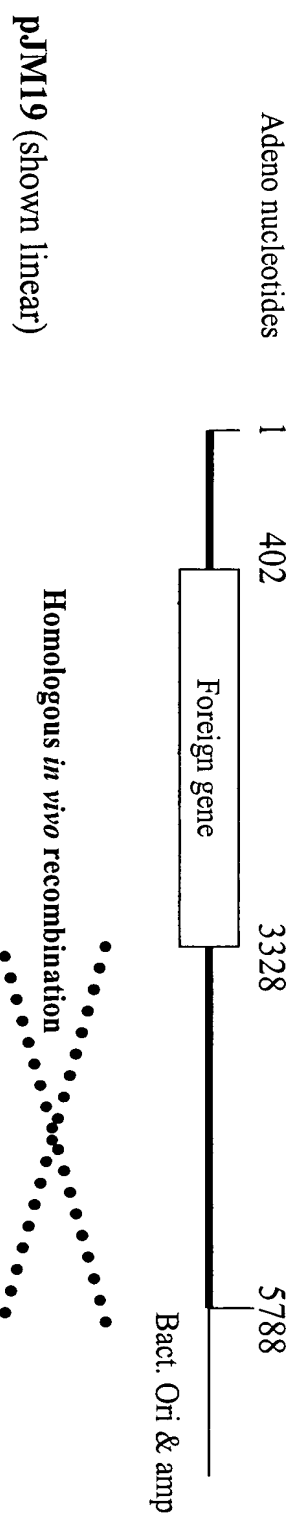
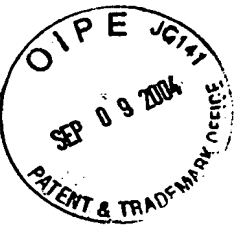
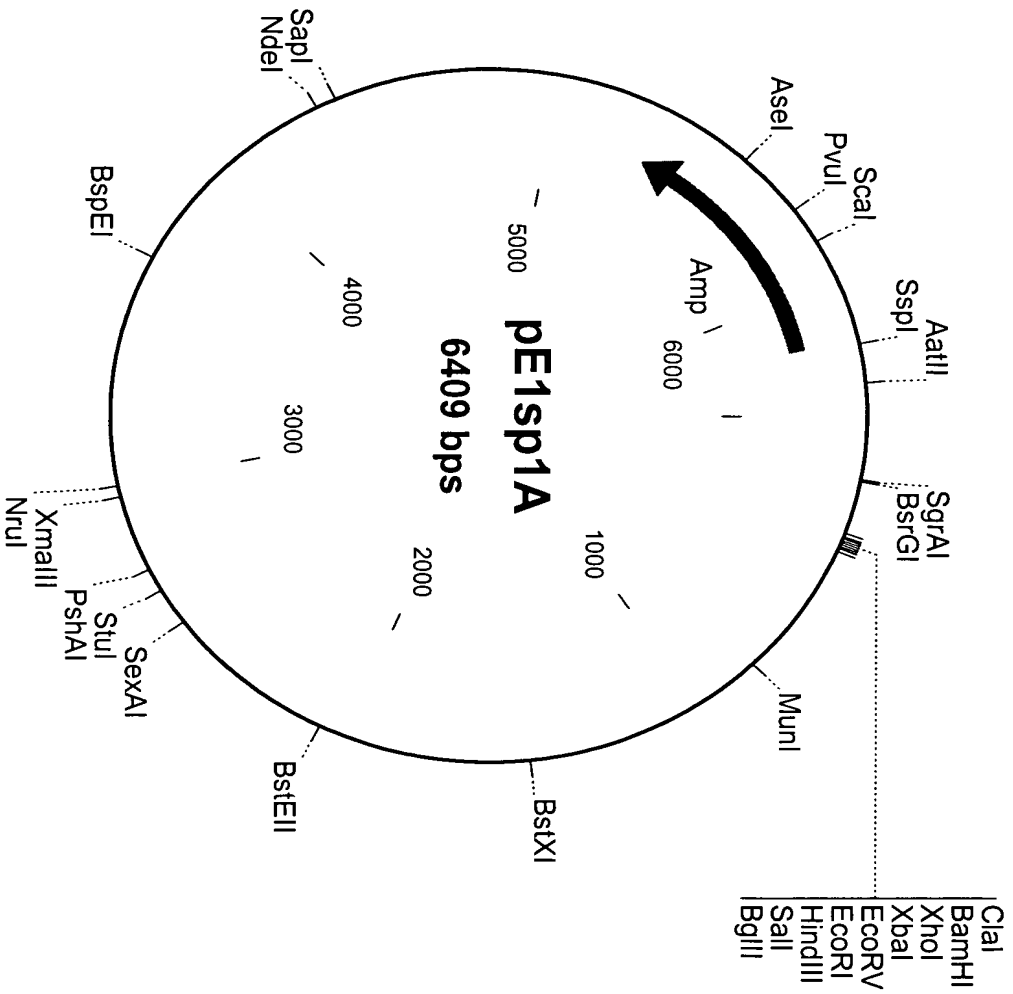


Figure 20



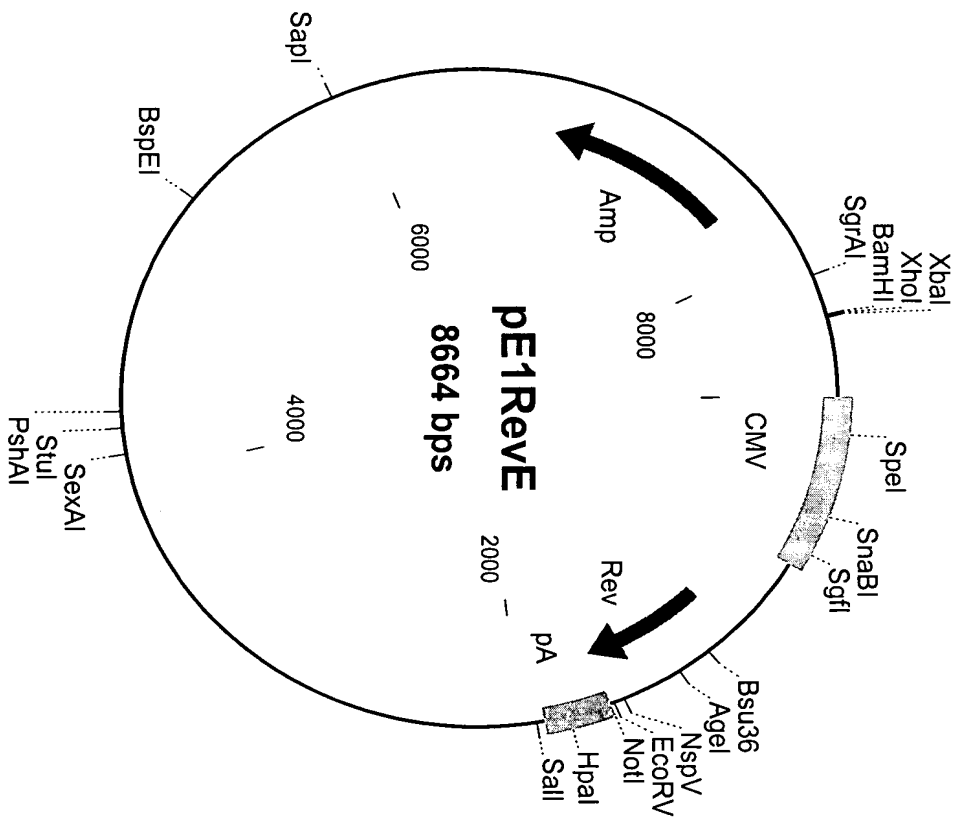
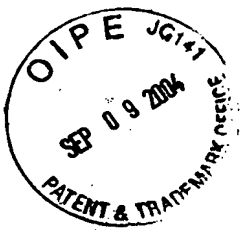


Figure 21

Figure 22

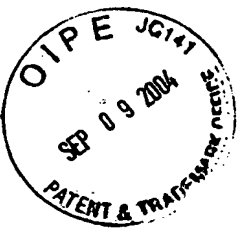
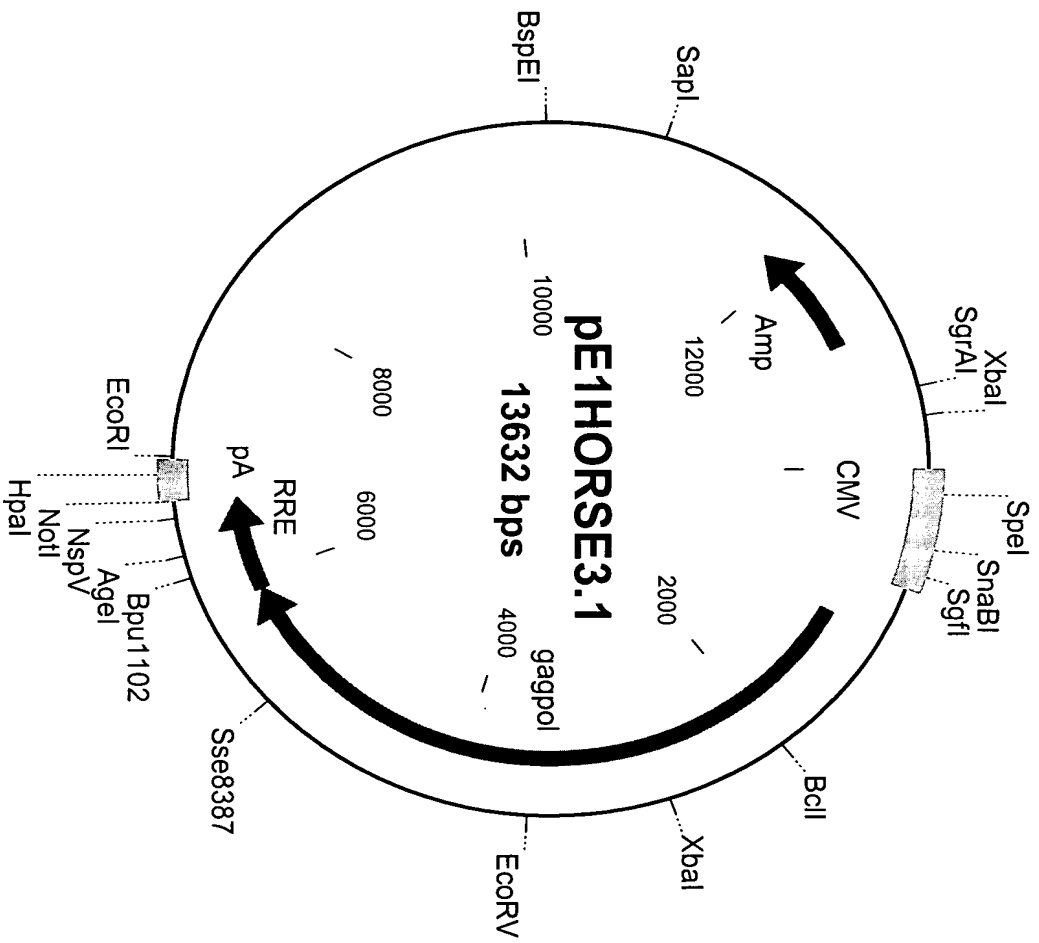


Figure 23

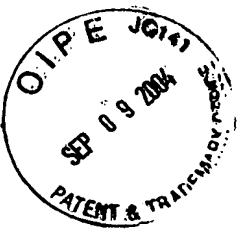
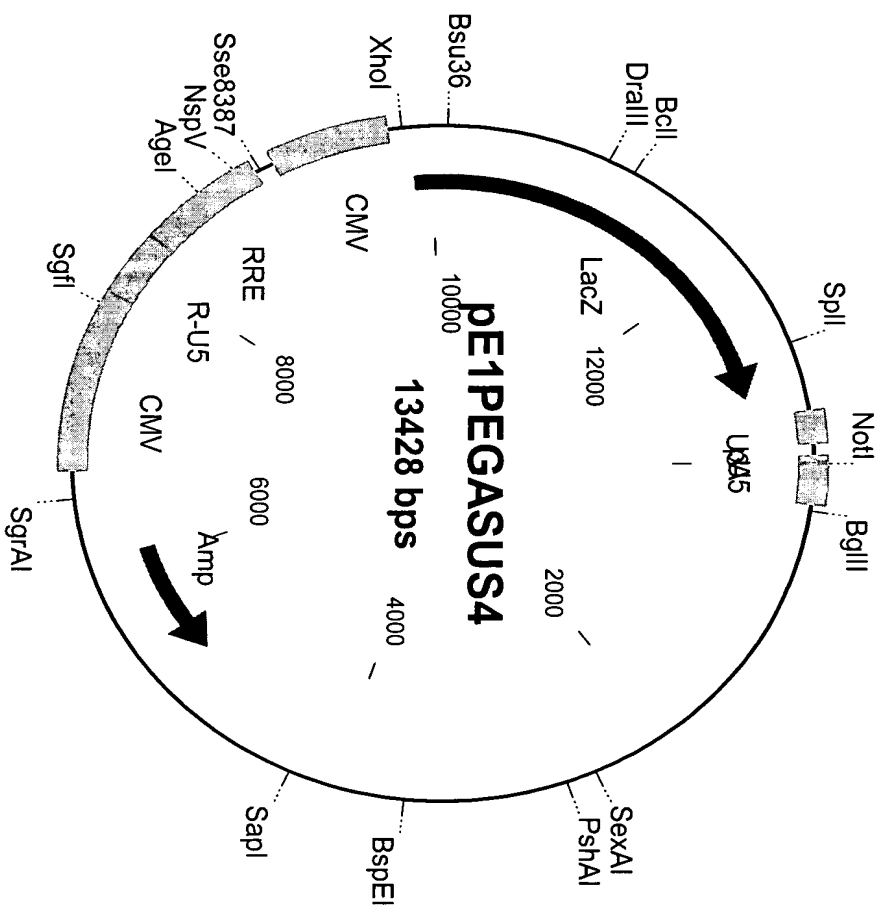




Figure 24

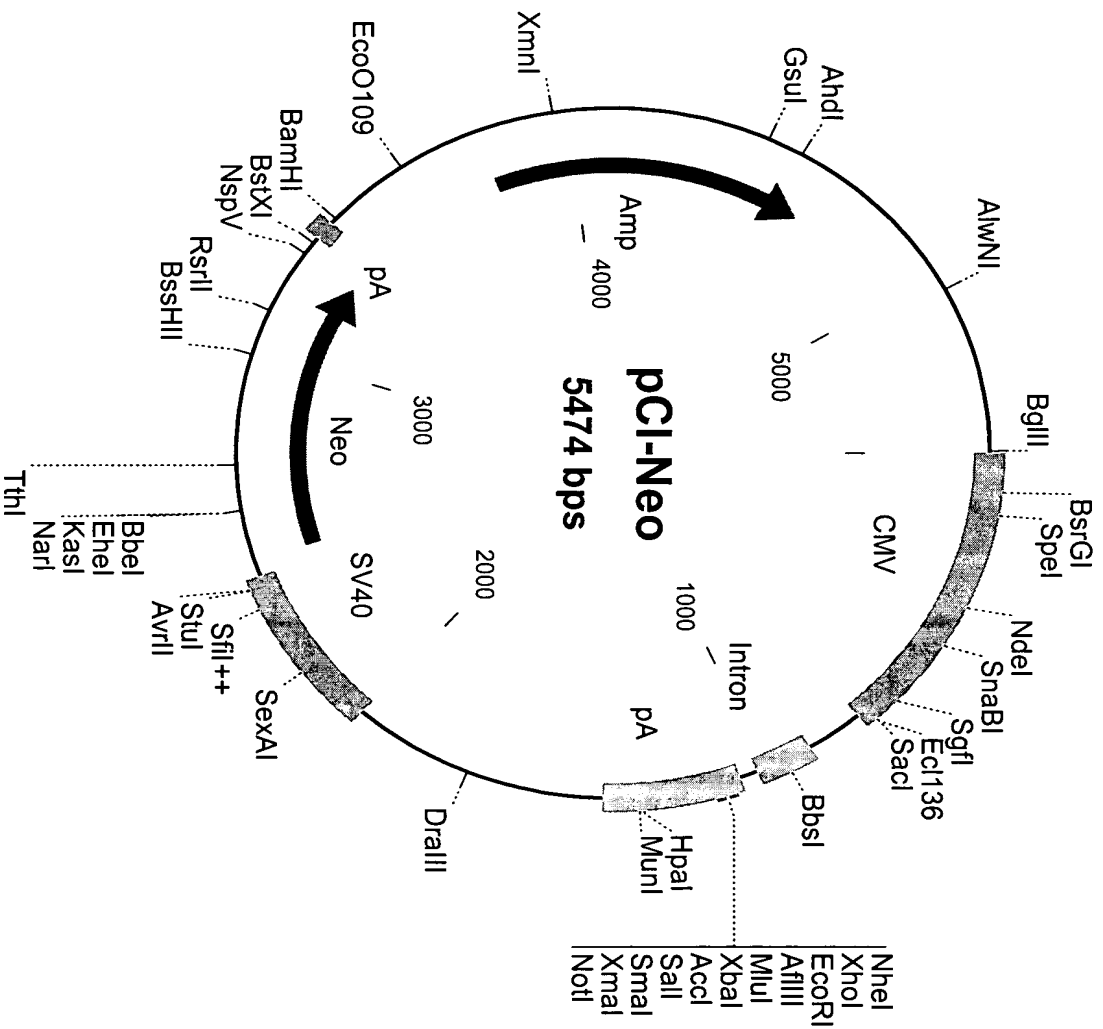
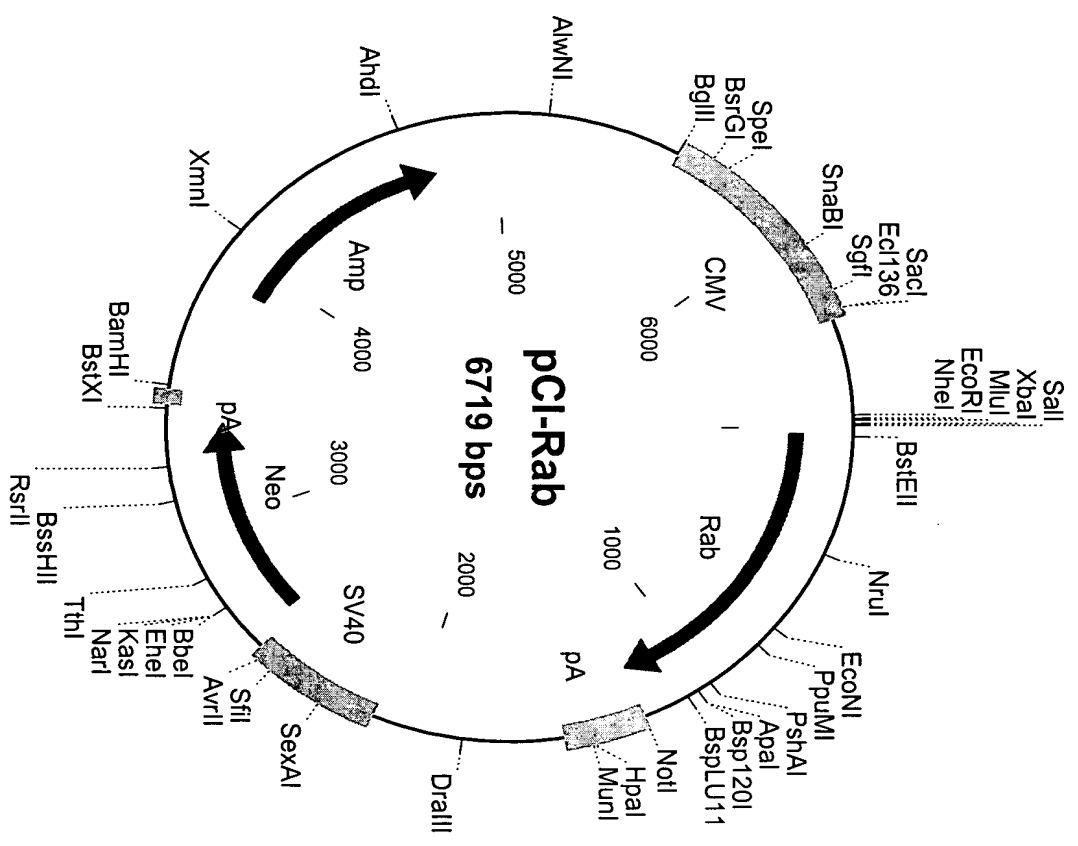


Figure 25



**Figure 26**

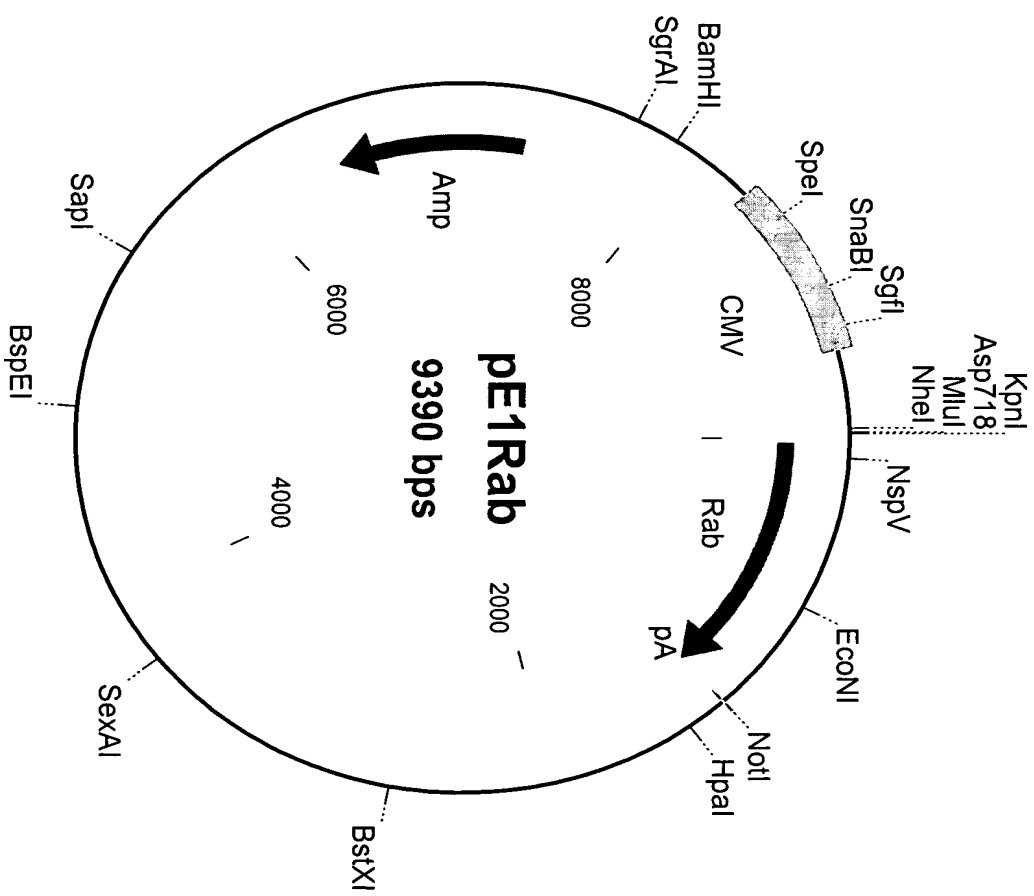
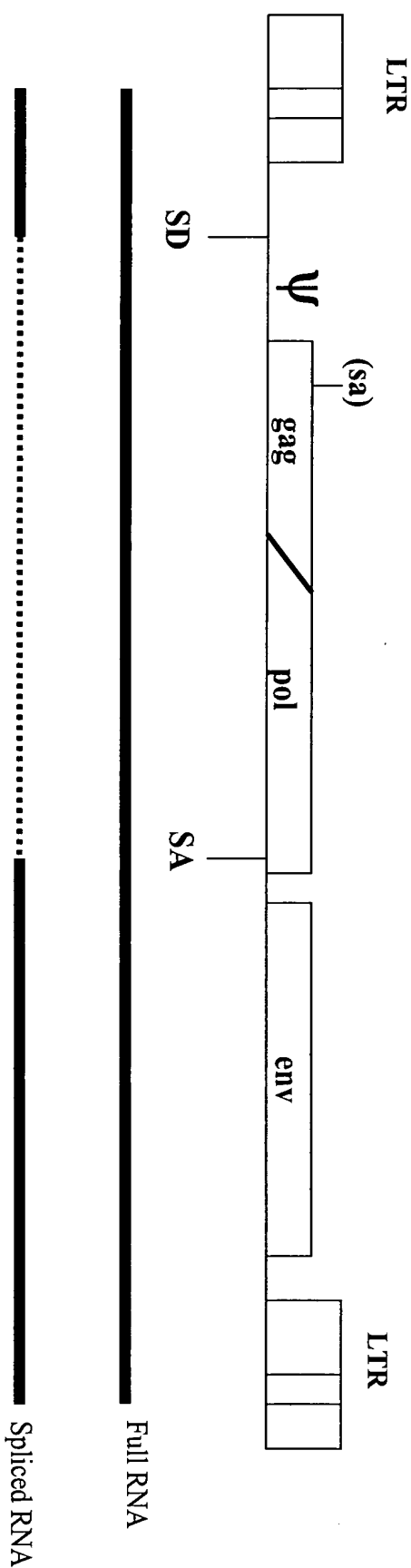


Figure 27a

A) Natural splicing configuration



SD = Splice donor

SA = Splice acceptor

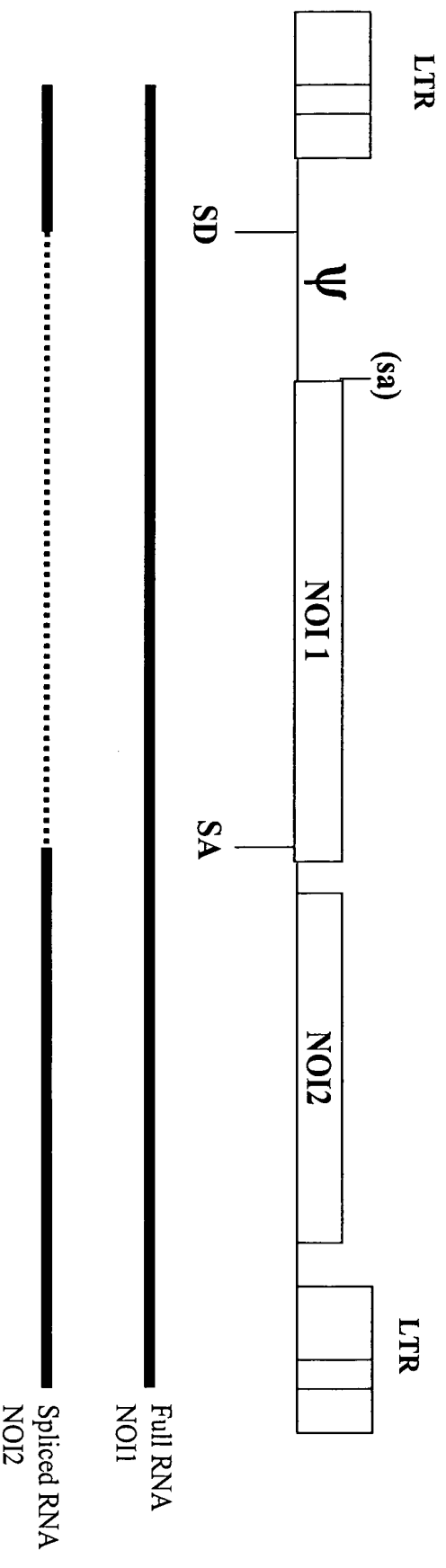
(sa) = cryptic splice acceptor

$\Psi$  = packaging site

Figure 27b

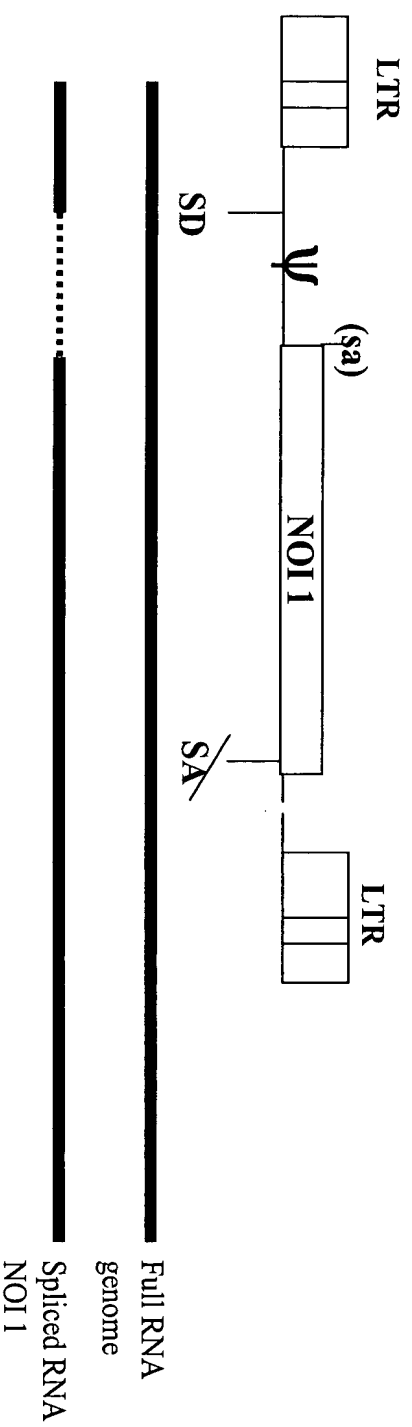
Splicing configurations in known vectors

e.g. LTRSVX



e.g. N2

Figure 27b cont.



e.g. MFG

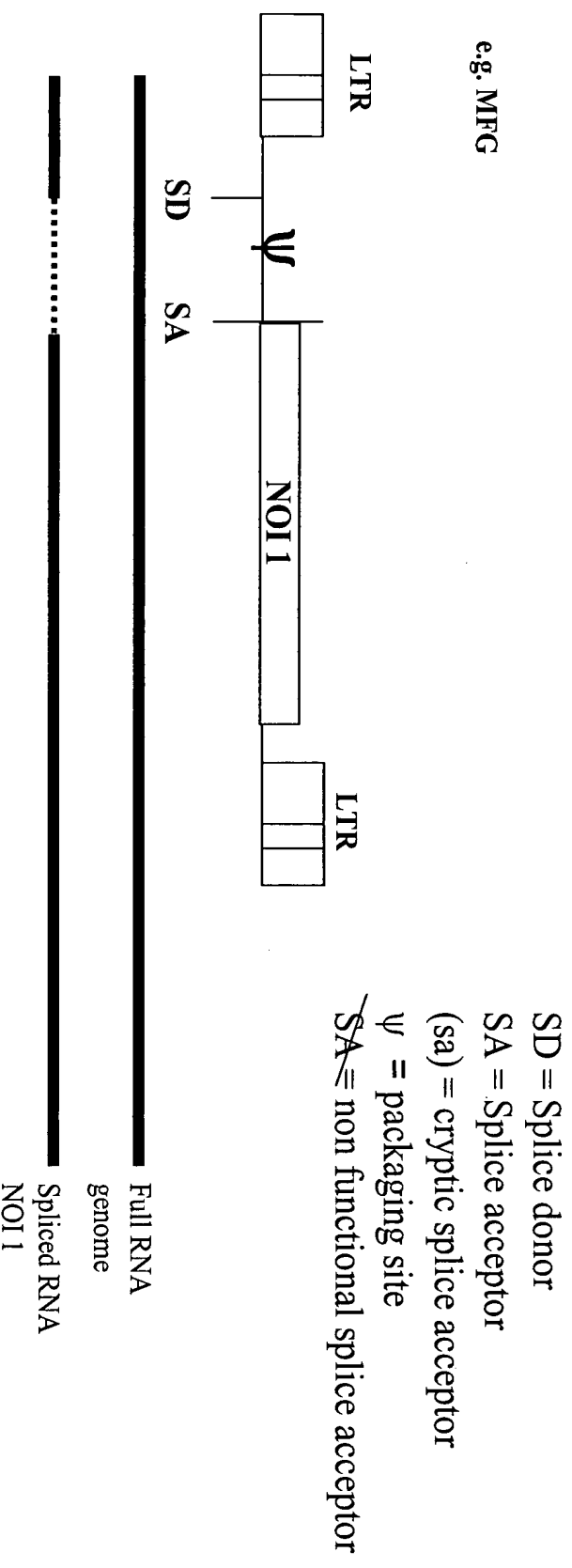
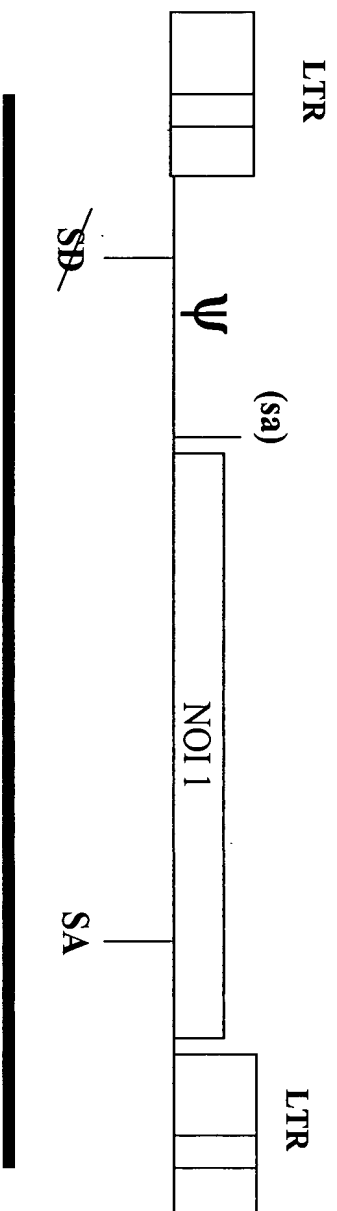


Figure 27b cont.

e.g pBABE



~~SD~~ = Non functional splice donor

SA = Splice acceptor

(sa) = cryptic splice acceptor

Ψ = packaging site

Full RNA  
genome and  
NOI 1

Figure 27c

SD = Splice donor  
~~SD~~ = non functional splice donor  
SA = Splice acceptor  
(sa) = cryptic splice acceptor  
 $\psi$  = packaging site  
IRES = internal ribosome entry site (optional)

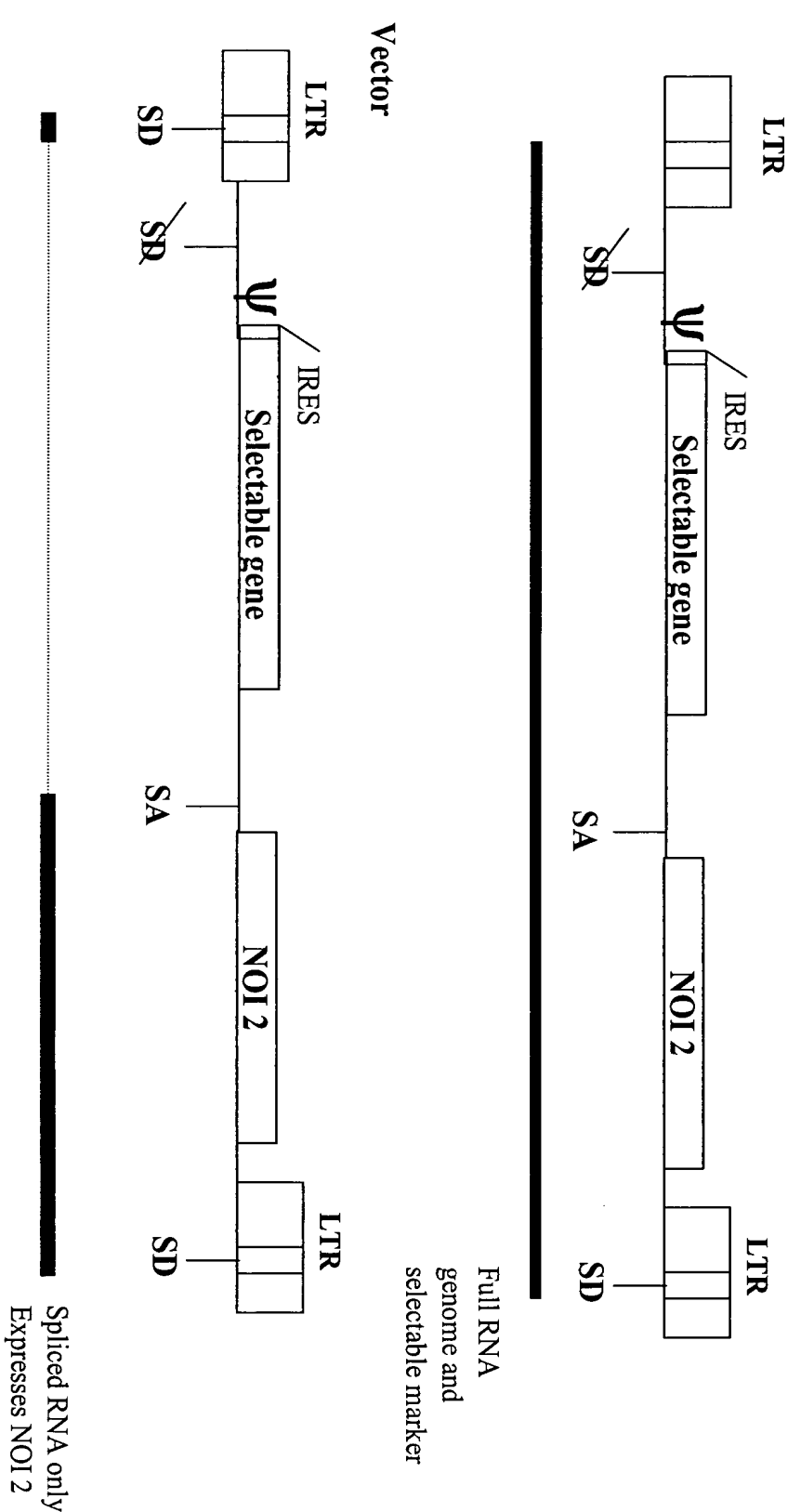
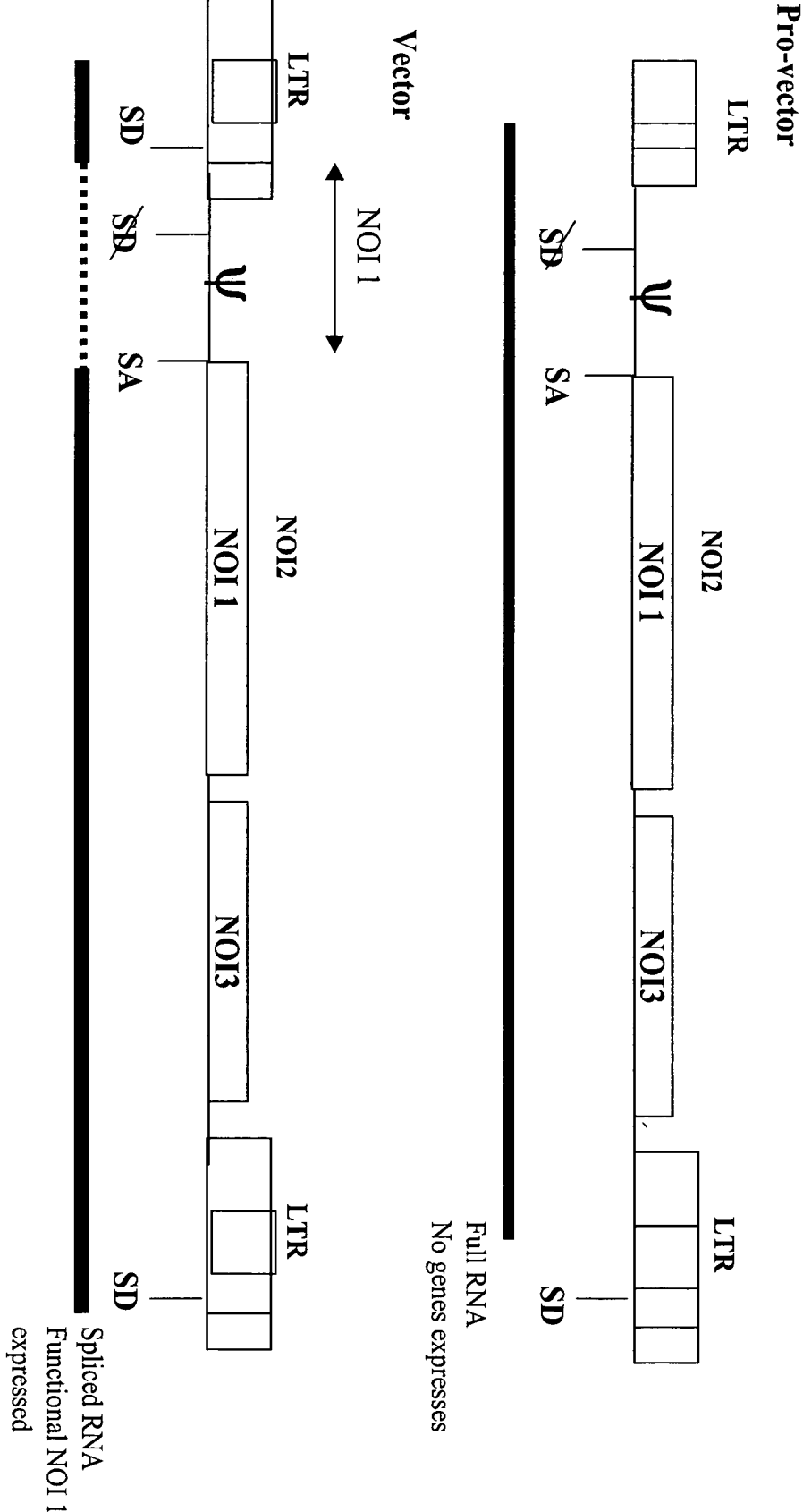




Figure 27c cont.



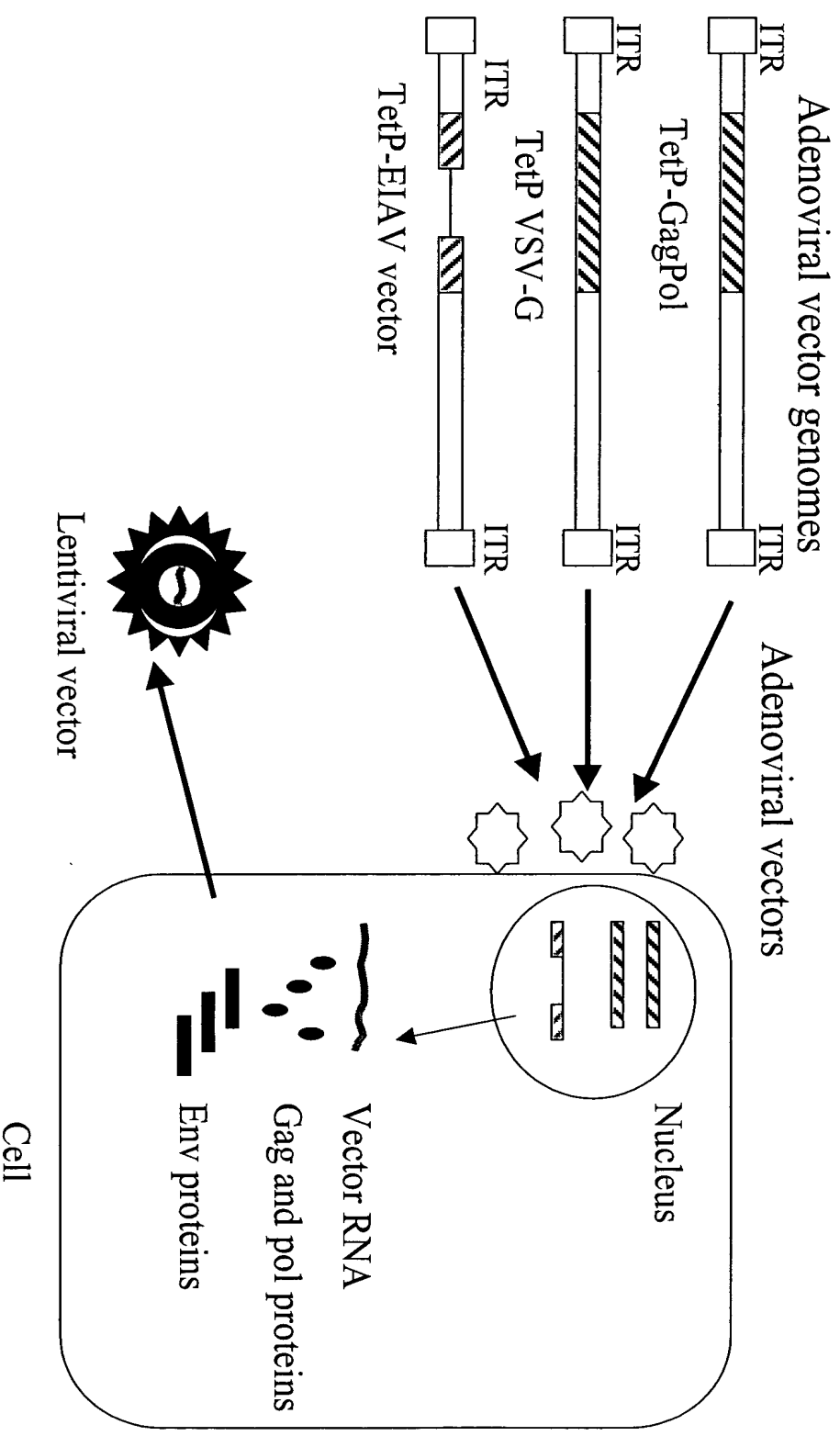


Figure 28

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